**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

Leveugle et al.

Serial No: 09/322,866

Filed: June 15, 1999

For: IMMUNOTHERAPETUIC COMPOSITION AND METHOD FOR THE TREATMENT OF PROSTATE CANCER

Art Unit: 1642

Attorney Docket No. AREX-P01-008

Examiner: M. DAVIS

Assistant Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

***Declaration Under 35 U.S.C. §1.132 of Birgit Schultes, Ph.D.***

I, Birgit C. Schultes, of Arlington, MA, hereby declare as follows:

1. I am the Vice President of Research at AltaRex Corporation and an inventor on the present application. I have been conducting research in tumor immunology for 14 years. Accordingly, my curriculum vitae is attached.

2. I have read the above-identified application, the pending claims, the Office Action mailed by the USPTO on December 3, 2002, and the Office Action mailed by the USPTO on February 27, 2002.

3. I understand that the Examiner has alleged that the invention as described and claimed in the above-identified application was not enabled. In particular, the Examiner alleges in the Office Action mailed February 27, 2002, that is it unpredictable that the claimed method could produce an immune response or antibody specific for prostate specific antigen in a host or a

patient having prostate cancer, in view of Example 12, wherein the treated mice have a tumor, and there is no therapeutic effect of the claimed antibody AR47.47.

Further, the Examiner alleges that since prostate specific antigen (PSA) is a self-antigen, it is unpredictable that in human patients with prostate cancer, the claimed antibodies would produce adequate numbers of cytotoxic T lymphocytes (CTLs) with high affinity which are optimal for interacting with the antigen.

Finally, with respect to Example 12, the Examiner alleges that one could not deduce from the fact that the claimed AR47.47 antibody induces anti-idiotypic antibodies against PSA in a prostate cancer-free host that the claimed AR47.47 antibody would also induce anti-PSA antibodies in a prostate cancer host.

I respectfully disagree with the Examiner's arguments.

4. To the extent the subject application describes the method of making Ab3 and Ab3', I do not believe that the data of Example 12 would be considered by scientists working in this field to teach away from the usefulness, nor suggest the methods of the pending claims were not fully enabled by the application. In particular, the animal model used in Example 12, as a model for prostate cancer in mice, differs from the expected progress of human prostate cancer. In mice, the disease progresses on a much more rapid timescale. Accordingly, the time frame of the experiment after initiation of treatment in that animal would be comparable to stages in the human disease that would generally be beyond effective treatment. Thus, the data of Example 12 is not, in general, indicative of either the likelihood of success or failure for treating human patients having prostate cancer. Rather, the animal model of Example 12 indicates that an immunotherapeutic approach may not be successful in very late stage disease when time to

induce an immune response is insufficient or the patient's immune system is highly suppressed due to the presence of large tumor burden would be understood simply to be irrelevant in that it does not reflect an appropriate model, and would not be taken as teaching away from the claimed methods.

5. Based on well-known principles, it could be readily understood by practitioners in this field that Ab3 antibodies induced by the administration of the claimed AR47.47 (Ab1) antibody would be highly specific for PSA. These antibodies can be generated via the idiotypic network or via processing of an immune complex of AR47.47 and PSA. According to the idiotypic network, the binding region of AR47.47 is immunogenic and can induce antibodies that fit exactly in the binding site of AR47.47 and consequently are mirror images of the respective PSA epitope of AR47.47 (Ab2). These Ab2 are in turn immunogenic and can induce antibodies that fit into their binding site. These Ab3 are mirror images of the Ab1 and bind to the same epitope as the Ab1. Therefore they have the same specificity as the Ab1, which has been demonstrated to be highly specific for PSA. Alternatively, AR47.47 can bind PSA in circulation and form an immune complex. Processing of these immune complexes can lead to production of PSA-specific antibodies that can bind to multiple epitopes on PSA or it can lead to activation of a cellular response to PSA. That PSA is a self-antigen is irrelevant with respect the claimed methods because the application describes a methods to break tolerance to a self antigen. It would have been expected at the time of filing that adequate numbers of CTLs with high affinity for PSA would be produced. That PSA is a self-antigen is irrelevant with respect to cancer therapy in general, and the claimed methods in particular.

By the time the present application was filed, one of ordinary skill in the art would readily deduce that if the claimed antibody AR47.47 could induced anti-idiotypic antibodies

against PSA, in a cancer free host, the claimed antibody would also be expected to induce anti-idiotypic antibodies against PSA in a host with prostate cancer. The presence or absence of PSA is irrelevant for induction of the idiotypic network and the production of Ab2 and Ab3. However, the presence of PSA, produced by the prostate cancer, is important for immune complex formation and induction of multiepitopic anti-PSA antibodies (Ab3') and T cells specific for PSA. Therefore is would be expected that anti-PSA antibodies could be more readily induced in a host with prostate cancer or in a host with residual disease.

6. I also understand that the Examiner has alleged that Example 11 is not an adequately predictive model of how the claimed method would perform in the treatment of human prostate cancer.

I respectfully disagree with the Examiner's comments.

7. In view of the entire teachings of the subject application, Example 11 can be related to the expected results in human prostate cancer. Patients suffering from prostate cancer are routinely treated, enter remission, and occasionally have residual disease in which PSA levels would rise. To prevent a relapse, an immunotherapeutic approach using AR47.47 would be very useful. The experiments given in Example 11 very closely mimic such a stage of prostate cancer. The tumors in mice grow at a much faster rate than prostate cancer does in humans, and would progress to an incurable stage within a few weeks. However, it takes at least three vaccinations or 6-8 weeks to induce a protective immune response in mice. Therefore, mice could not be immunized sufficiently if immunizations were started after implantation of the tumor. Therefore, the mice in example 11 were administered the Ab1 prior to tumor inoculation to present an adequate model of early human prostate cancer or human prostate cancer after

primary treatment. No one skilled in the art would believe that complete remission in 100 percent of the animal models would be required in order to expect the subject treatment to be useful in human patients. To the extent a patient experiences a recurrence of the disease, it would be expected that they could be re-treated with AR47.47Ab1 antibodies to cause the patient to re-enter remission or may need to seek combination with alternative therapies. Ab3 induced by the renewed treatment would bind to newly formed tumor cells.

8. I understand the Examiner has alleged that it is not clear from experiments 8, 13, 10, and 14 that Ab3 are produced. Further, I understand the Examiner has alleged that in experiments 8, 10, and 14, the negative controls have positive results for Ab3 and has argued the results make it unpredictable as to whether Ab3 is actually detected in the reported experiments.

I respectfully disagree with the Examiner's comments.

9. The "positive results" the Examiner points to in the negative controls of experiments 8, 10, and 14 are likely the result of an immunological reaction of the mice to injection of a xenogeneic tumor cell line. The PSA expressed by the tumor cell line is foreign to the mice and consequently, mice produce antibodies to PSA as a result of tumor inoculation. Thus, it is not surprising or unexpected that some antibodies are present in the background of the negative controls. However, in successful experiments, the level of anti-PSA antibodies should be much higher than in controls, and that observation does not alter the overall teachings of the subject application. In experiments 8, 10 and 14, AR47.47 did not induce a protective immune response in the majority of animals, indicated by the fact that antibody titers are not higher in AR47.47 treated mice than in the control animals. This is likely due to the fact that tumor was implanted prior to the immunizations and consequently time was insufficient to immunize the mice

appropriately. The finding underlines that it is important that treatment with AR47.47 induces a protective immune response. Without that, the treatment has no effect on tumor progression. That observation does not teach away from the disclosure of the instant application. No one skilled in the art would believe that complete remission in 100 percent of the animal models would be required in order to expect the subject treatment to be useful in human patients. More importantly, evaluation of different treatment schedules allows for selection of an appropriate cancer population. For AR47.47 treatment, the experimental data indicate that this treatment would be most useful in early stage disease or as an adjunct treatment after first-line therapy, but unlikely to be successful in late stage disease.

10. I understand the Examiner has alleged that the presence of Ab2 does not correlate with the claimed methods for inducing an immune response to PSA in a patient, or for inducing a host to produce an Ab3 that specifically binds to PSA. I understand further, that the Examiner has alleged that the claims do not recite a method for inducing the production of Ab2 antibodies.

I respectfully disagree with the Examiner's comments.

11. By the time the present application was filed, the anti-idiotypic network was well-known and accepted in the art in that administration of Ab1 antibodies induced the formation of Ab2 antibodies, which ultimately induced the formation of Ab3 antibodies in a patient. The methods of the pending claims rely on this phenomenon and but also represent an advancement over the art in the realization that the induction of an anti-idiotypic network generating anti-PSA antibodies includes not only Ab3, but also Ab3', which are induced by complexes of AR47.47 and tumor-antigens, such as PSA. The Ab3' response is a subset of an anti-PSA response where

the anti-PSA antibodies recognize epitopes distinct from the Ab1 antibody on a multi-epitopic antigen such as PSA.

In view of the teachings of the subject application, it is my expectation that Ab3 and Ab3' antibodies would be successfully generated by the administration of Ab1 antibodies, and would bind to an epitope on circulating prostate specific antigen in a patient. The induction of Ab2 and Ab3 antibodies in other settings was routine in the art at the time of filing, and I would not have expected that any undue experimentation would be required to induce Ab2 and Ab3 antibodies by the claimed method. Further, induction of Ab2 and Ab3 by the claimed method has clearly been demonstrated throughout the application (see Examples 5, 6, 8, 10, and 11). As is disclosed in Example 10 of the application, a competitive binding assay demonstrated the presence of both Ab2 and Ab3 antibodies as also indicated by the competitive assays of Examples 7, 9, 11 and 12 (see page 32 of the instant application). Thus, the experimental results observed indicate that Ab3 were successfully produced. Further, based on the state of the art at the time of filing and the disclosure of the specification as filed, I would reasonably expect production of Ab3 and Ab3' as a consequence of the anti-idiotypic network. The Examiner's allegation that the claims do not recite a method for inducing the production of Ab2 antibodies, and ultimately Ab3 and Ab3' antibodies, is therefore incorrect.

12. I understand that the Examiner alleges that one would not have expected any significant amount of tumor-specific antibody (Ab3) would be produced in a host with a pre-existing tumor burden.

I respectfully disagree with the Examiner's comments.

13. By the time the present application was filed, it was well-known and accepted in the art that when Ab1 antibodies are administered to a patient, Ab2 and Ab3 antibodies are induced in a host with tumor burden. This has been demonstrated by several investigators, such as PB Chapman (*Semin Cancer Biol.* 6(6): 367-374 (1995); Exhibit A) and Herlyn et al. (*Cancer Immunol Immunother* 43(2): 65-76 (1996); Exhibit B).

An unexpected feature disclosed in the instant application over the prior art was that multi-epitopic Ab3 and Ab3' responses to the tumor-associated antigen PSA could be produced. Based upon the teachings of the specification, I would have concluded at the time of filing that multi-epitopic Ab3 and Ab3' antibodies would be produced in a host, and would have a therapeutic benefit for the host.

14. As one of skill in the art at the time the invention was made, I believe that the disclosure as a whole teaches one skilled in the art how to make and use the invention as claimed.

15. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Birgit Schultes

Dated: 5/30/03 Signature: 

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## EMPLOYMENT HISTORY

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| 2003 - present | **Vice President**, Research<br>AltaRex Corp. |
| 2001-2002 | **Exec. Director,** Research and Clinical Immunology<br>AltaRex Corp |
| 1998-2000 | **Director,** Preclinical Research<br>AltaRex Corp |
| 1996-1998 | **Scientist and Senior Scientist**, Research & Development<br>AltaRex Corp. |
| 1995-1996 | **Research Associate**, Research & Development<br>Biomira Inc. |
| 1994-1995 | **Postdoctoral Fellow**, Research & Development<br>Biomira Inc. |
| 1990-1993 | **Supervisor**, Clinical Chemistry, Tumor Marker Laboratory<br>Clinic of Nuclear Medicine, University of Bonn, Germany |

## EDUCATION

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|---|---|
| 1989-1993 | Ph.D., summa cum laude, Major: Cell Biology/Immunology, Minor: Biochemistry<br>University of Bonn, Germany, Department of Cell Biology (Prof. V. Herzog), Studies of the idiotypic network in responses to anti-CA125 Mab-OC125 in patients and animal models. |
| 1982-1989 | M.Sc. in Biology (Major: Genetics, Minor: Cell Biology, Biochemistry)<br>University of Bonn, Germany and University of Cologne, Germany, Thesis on purification and characterization of an enzyme that regulates DNA metabolism. |

## MEMBERSHIP OF SCIENTIFIC SOCIETIES

American Association for Cancer Research
American Association of Immunologists
American Society of Photobiology
Society of Tumor Targeting

## PROFESSIONAL EXPERIENCE

*ALTAREX CORP., EDMONTON, AB, CANADA AND WALTHAM, MA (1996 TO PRESENT)*

**Vice President, Research and Exec. Director, Research and Clinical Immunology (2001 to present)**

Responsible for directing discovery and preclinical research activities related to AltaRex's technology. Studies are focussed on the function of AltaRex antibody products to induce or inhibit immune responses (in particular T cell responses) to cancer antigens, viruses, autoimmune targets and allergens using dendritic cell systems and a variety of functional T cell assays. Besides investigations into immune modulation mechanisms, my group is responsible for improvements of the technology, proof-of concept in cell-based assays and animal models, validation of assays and systems, and preclinical studies for toxicology, immunohistochemistry and pharmacokinetics. Studies performed in-house as well as outsourced to CRO and academic institutions.

Responsibilities include:

- Supervision and direction of a team of scientists to delineate the mechanism of action of AltaRex's antibody candidates and built a technology platform with applications in cancer, viral infections, allergy and autoimmune diseases. This work mainly focuses on T cell immunology involving antigen processing by dendritic cells and T cell activation in response to antigens and antigen-antibody complexes using ELISPOT, intracellular cytokine staining, cytokine assays, receptor studies and signal transduction pathways.
- Preclinical testing of cancer product candidates in animal models, pharmacokinetic, pharmacodynamic, immunohistochemnistry and toxicology studies
- Assay development, optimization and validation of assays for analysis of immune responses in patients in clinical trials with AltaRex's cancer vaccines, management of on-site validation and clinical sample analysis (ELISAs, ELISPOT, T cell proliferation, cytotoxic assays) at outside contract labs (Dr. Whiteside, University of Pittsburgh)
- Development, optimisation and qualification of bioassays
- Management of the Clinical Immunology program and integration of timelines with the clinical team, assistance with clinical trial design and protocols
- Establishment and coordination of research collaborations with academia, contract negotiations, MTAs
- Establishment and coordination of preclinical testing with preclinical research organizations, contract negotiations, agreements
- Cooperation with Business Development and Finance in partnering meetings with representatives of the pharmaceutical industry or venture capital firms to present the company's scientific platform
- Presentations at scientific meetings, management of the scientific advisory board including organization of Scientific Advisory Board meetings; participation in meetings with the FDA

- Preparation of preclinical reports, BLA preparation, SOPs, budgets, GLP training, publications; principle investigator for animal experiments and Radionuclide Use

Directly reporting staff includes managers (Ph.D.), scientists (Ph.D.), and senior technicians; total reports: 6-10.

**Director, Preclinical Research (April 1998 to Dec. 2000)**

Responsible for generation and characterization of new antibodies, biological evaluation of novel cancer vaccines in animal model and *in vitro* studies, assay development and validation, preclinical testing of drug candidates for toxicology, pharmacodynamics, immunohistochemistry and pharmacokinetics.

Responsibilities include:

- Supervision and direction of hybridoma technology in generating new hybridoma clones against cancer antigens and inflammation targets as well as anti-idiotypic antibodies; characterization of antibodies for specificity, cross-reactivity, affinity, epitope mapping and physicochemical properties
- Animal model development, including human-PBL-SCID/bg mouse models, nude mouse, transfectoma and transgenic mouse or rat models for various tumors and rheumatoid arthritis
- Preclinical testing of product candidates for pharmacokinetic, pharmacological and toxicology studies in mice, rats, rabbits and primates; coordination of studies with preclinical research organizations
- Recombinant DNA technology: fusion proteins of scFv antibodies with various effector functions like cytokines and receptors on antigen-presenting cells, phage display libraries
- Assay development, optimization and validation of assays for analysis of product characteristics and pharmacological properties of AltaRex's cancer vaccines in clinical trial patients
- Preparation of INDs, protocols and investigator brochures for clinical trials
- Presentations at scientific meetings and partnering meetings with representatives of the pharmaceutical industry; participation in meetings with the FDA; writing of SOPs, reports, publications; preparation of animal protocols; principle investigator for animal experiments and Radionuclide Use

Directly reporting staff included senior scientists, scientists, technicians and students; total reports: 15

**Senior Scientist, Research and Development (1997 to March 1998)**

Responsible for development of targeted photodynamic therapy with direct report to Vice President Research and Development. The responsibilities included project management of an immunoliposomal formulation of a photosensitizer to treat solid tumors, coordinating process development and scale-up for hypocrellin (photosensitizer) synthesis, formulation work into antibody-coated liposomes, assay development, biological evaluation (*in vitro* and *in vivo*) of various hypocrellin formulations and development of animal models. The project was sponsored by IRAP.

**Scientist, Research and Development (1996-1997)**

Responsible for clone development, assay development and *in vitro* characterization of two of AltaRex cancer vaccines (for breast and gastro-intestinal cancer)

Responsibilities included supervision of the hybridoma lab in generating new clones for cancer antigens and their characterization for specificity, epitope mapping and affinity, initial evaluation of clones for stability and productivity; testing of their therapeutic activity in various mouse tumor models, supervision of assay development for immunological assays (humoral and cellular) for research and clinical trial support, development, optimization and validation of assays for product quantification and qualification; characterization of antibodies, pharmacokinetic studies; and studies on the immune responses induced by AltaRex cancer vaccines. Additional responsibilities included writing of SOPs, reports, publications, management of the lab.

*BIOMIRA INC., EDMONTON, AB, CANADA (1994-1995)*

**Research Associate, Research and Development (1995)**
Responsible for studies on the immunological mechanisms of action of OvaRex® MAb-B43.13 for ovarian cancer with direct report to the Director of Research. Additional responsibilities included antibody *in-vitro* characterization, assay development for immunoreactivity testing of monoclonal antibodies, clinical immune response quantification and for quantification of OvaRex® MAb-B43.13 in pharmacokinetic studies in patients, and analysis of serum and lymphocyte samples from clinical trials.

**Postdoctoral Fellow, Research and Development (1994)**
Responsible for studies on the B and T cell activation of immune complexes consisting of an antibody against ovarian cancer and the CA125 tumor-associated antigen *in vitro* and *in vivo*..

*UNIVERSITY OF BONN, BONN, GERMANY (1989-1993)*

**Research Assistant, Clinic for Gynecology and Obstetrics (1989-1993)**
Studies on antibody-coupled phthalocyanine for photodynamic therapy

**Supervisor, Clinic for Nuclear Medicine (1990-1993)**
Responsible for tumor marker laboratory.

## PUBLICATIONS

*ORIGINAL ARTICLES IN PEER-REVIEWED JOURNALS*


**B.C. Schultes** and T.L. Whiteside. Monitoring of Immune Responses to CA125 with an IFN-γ ELISPOT Assay. J. Immunol. Methods, in press

V.J. Moebus, R.P. Baum, M. Bolle, R. Kreienberg, A.A. Noujaim, **B.C. Schultes**, C.F. Nicodemus. Immune responses to MAb-B43.13 correlate with prolonged survival of women with recurrent ovarian cancer. Am. J. Obstet. Gynecol., in press

J.S. Berek, **B.C. Schultes**, C.F. Nicodemus. Biologic and imunologic therapies for ovarian cancer. J. Clin. Oncol. 21, 168-174, 2003

C.F. Nicodemus, **B.C. Schultes**, B.L. Hamilton. Immunomodulation with antibodies: clinical application in ovarian cancer and other malignancies. Expert Rev. Vaccines 1(1), 35-48, 2002.

W. Qi, **B.C. Schultes**, D. Liu, M. Kuzma, W. Decker, A.A. Noujaim, R. Madiyalakan. Characterization of an anti-MUC1 monoclonal antibody with potential for immunotherapy of cancer. Hybridoma and Hybridomics 20, 313-323, 2001

K.A. Berlyn, **B.C. Schultes**, B. Leveugle, A.A. Noujaim, R.B. Alexander, and D.L. Mann. Generation of CD4+ and CD8+ T Lymphocyte Responses by Dendritic Cells Armed with PSA/anti-PSA (antigen:antibody) Complexes. Clin. Immunol. 101, 276-283, 2001

A.A. Noujaim, **B.C. Schultes**, R.P. Baum, R. Madiyalakan. Antibody-Mediated Immunotherapy: Influence of Circulating Antigen on the Induction of Antigen-Specific Anti-Tumor Immune Responses. Cancer Biotherapy&Radiophar., 16, 187-203, 2001

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P.D. Rye, N.V. Bovin, E.V. Vlasova, A.A. Molodyk, A. Baryshnikov, F.T. Kreutz, W.I. Garinther, **B.C. Schultes**, A.A. Noujaim, R. Madiyalakan, J. Magnani, et al. Summary Report on the ISOBM TD-6 Workshop: Analysis of 20 Monoclonal Antibodies against Sialyl Lewis$^a$ and Related Antigens. Tumor Biol. 19, 390-420, 1998.

**B.C. Schultes**, R.P. Baum, A. Niesen, A.A. Noujaim, R. Madiyalakan. Anti-Idiotype Induction Therapy: Anti-CA125 Antibodies (Ab3) Mediated Tumor Killing in Patients Treated with Ovarex MAb-B43.13 (Ab1). Cancer Immunol. Immunother. 46, 201-212, 1998.

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R. Madiyalakan, R. Yang, **B.C. Schultes**, R.P. Baum, A.A. Noujaim. OVAREX MAb-B43.13: IFN-gamma Could Improve the Ovarian Tumor Cell Sensitivity to CA125-Specific Allogenic Cytotoxic T Cells. Hybridoma 16: 41-45, 1997.

A. Schomburg, F. Grunwald, **B. Schultes**, A. Hotze, H. Bender, H.J. Biersack. Are Serum Neopterin Concentrations Superior to other Parameters in the Differential Diagnosis and Prognosis Assessment of Graves' Disease? Exp. Clin. Endocrin. Diabetes 104: 123-129, 1996

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**B. C. Schultes**, J. Reinsberg, H. Schlebusch, P. Oehr, H.J. Biersack, D. Krebs, and U. Wagner. Idiotypic Cascades in a Mouse Model treated with the Monoclonal Antibody OC125. Induction of Anti-CA 125 Antibodies after Immunization with an Anti-CA 125 (MAb OC125) Antibody by the Activation of the Idiotypic Network. Eur. J. Clin. Chem. Clin. Biochem.31: 427-432, 1993

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**B.C. Schultes**, E. Fischbach, N. Dahlmann. Purification and characterization of two different thymidine-5'-triphosphate-hydrolyzing enzymes in human serum. Biol. Chem. Hoppe-Seyler 373, 237-247, 1992

S. Schmidt, **B. Schultes**, U. Wagner, P. Oehr, W. Decleer, H. Lubaschowski, H.J. Biersack and D. Krebs. Photodynamic laser therapy of carcinomas - effects of five different photosensitizers in the colony-forming assay. Arch. Gynecol. Obstet. 249, 9-14, 1991

J.M. Pollok, **B. Schultes**, P. Oehr. Labelling of a Biotin-Derivative by 99mTc, its Purification and Binding-Capacity to Avidin. NucCompact 21, 36-37, 1990

P. Oehr, Q. Liu, U. Loos, **B. Schultes**, H.J. Biersack. NSE and TPA: Significance of simultaneous determination for follow-up of lung cancer. Journal of Tumor Marker Oncology 1990

**B.C. Schultes** and N. Dahlmann. Homogeneous preparation of human thymidine-5'-triphosphatase by electroelution from SDS/PAGE with subsequent renaturation. Eur. J. Biochem. 192, 201-205, 1990

*CONTRIBUTIONS TO BOOKS*

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**B. Schultes**, H.J. Biersack, S. Schmidt, U. Wagner, D. Krebs. Akkumulation von Antikörper-Farbstoff-Isotopen-Komplexen - Tierexperimentelle Untersuchungen zur photodynamischen Lasertherapie. in Krebs und Berg (Hrsg.), Archives of Gynecology and Obstetrics, Springer, Berlin, Heidelberg, New York, London, Paris, Tokyo, Hong Kong, Barcelona, Budapest, in press, 1993.

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## *ABSTRACTS, PRESENTATIONS, POSTERS AT SCIENTIFIC MEETINGS*

**B.C. Schultes,** M.L. Kuzma, C.C. Zarozinski, K. Agopsowicz, H. Eng. Uptake and processing of antigen-antibody-complexes by human dendritic cells: involvement of multiple receptors and in particular the mannose receptor. AAI Annual Meeting, May 6-10, 2003, Denver, CO/.

**B. Schultes**, A.N. Gordon, C.F. Nicodemus, T.L. Whiteside. Feasibility of combined OvaRex® immunotherapy and chemotherapy in recurrent ovarian cancer. AACR Annual Meeting, rescheduled for July 11-14, 2003, Washington, DC.

J.L. Levin, J. Kavanagh, C. Nicodemus, **B. Schultes**, E. Hansen, M. Method. Immunology and pharmacokinetic comparability profiles of OvaRex® (MAb-B43.13) in women with ovarian cancer. AACR Annual Meeting, rescheduled for July 11-14, 2003, Washington, DC.

**B.C. Schultes.** Antibodies to modulate tumor immunity. Cancer Drug Development, SMi, March 10-11, 2003, London, UK

H. Eng, M.L. Kuzma, K. Agopsowicz, C.C. Zarozinski, **B.C. Schultes.** Complexation with Murine MAb-B43.13 Alters the Endocytic Trafficking of the Mucinous Tumor Antigen CA125 after Uptake by Human Dendritic Cells. Keystone Symposium "Dendritic Cells: Interfaces with Immunobiology and Medicine", March 3-8, 2003, Keystone, CO.

K. Agopsowicz, M. Kuzma, H. Eng, C.C. Zarozinski, **B.C. Schultes.** Opsonization with specific antibodies enhances dendritic cell presentation of apoptotic tumor cells and induction of CTL. Keystone Symposium "Cell Biology of the Immune Response", March 5-10, 2003, Keystone, CO.

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